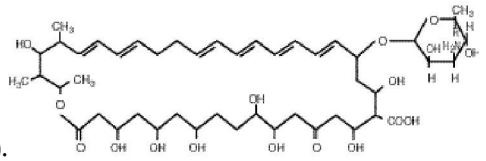
**NYSTATIN AND TRIAMCINOLONE ACETONIDE - nystatin and triamcinolone acetonide cream**
E. FOUGERA & CO., A division of Nycomed US Inc.

**Rx ONLY**
**FOR DERMATOLOGIC USE ONLY**
**NOT FOR OPHTHALMIC USE**

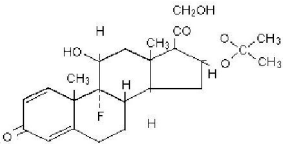
## DESCRIPTION

Nystatin and triamcinolone acetonide cream for dermatologic use contains the antifungal agent nystatin and the synthetic corticosteroid triamcinolone acetonide.

Nystatin is a polyene antimycotic obtained from *Streptomyces noursei.* It is a yellow to light tan powder with a cereal-like odor, very slightly soluble in water, and slightly to sparingly soluble in alcohol. It has a molecular formula of $C_{47}H_{75}NO_{17}$ and a molecular weight of 926.13 (CAS Registry Number 1400-61-9).



Triamcinolone acetonide is designated chemically as pregna-1,4-diene-3,20-dione, 9-fluoro-11,21-dihydroxy-16,17-[(1-methylethylidene)bis(oxy)]-, (11β,16α)-. The white to cream crystalline powder has a slight odor, is practically insoluble in water, and very soluble in alcohol. It has a molecular formula of $C_{24}H_{31}FO_6$ and a molecular weight of 434.50 (CAS Registry Number 76-25-5).



Each gram of nystatin and triamcinolone acetonide cream USP contains 100,000 USP Nystatin Units and 1 mg of triamcinolone acetonide in a cream base containing polyoxyethylene fatty alcohol ether, white petrolatum, glyceryl monostearate, polyethylene glycol 400 monostearate, sorbitol solution, si-methicone emulsion, propylene glycol, aluminum hydroxide gel, polysorbate 60, titanium dioxide, and purified water with benzyl alcohol as a preservative. Hydrochloric acid or sodium hydroxide to adjust pH.

## CLINICAL PHARMACOLOGY:

### NYSTATIN

Nystatin exerts its antifungal activity against a variety of pathogenic and nonpathogenic yeasts and fungi by binding to sterols in the cell membrane. The binding process renders the cell membrane incapable of functioning as a selective barrier. Nystatin provides specific anticandidal activity to *Candida* (Monilia) *albicans* and other *Candida* species, but it is not active against bacteria, protozoa, trichomonads, or viruses. Nystatin is not absorbed from intact skin or mucous membranes.

### TRIAMCINOLONE ACETONIDE

Triamcinolone acetonide is primarily effective because of its anti-inflammatory, anti-pruritic and vasoconstrictive actions, characteristic of the topical corticosteroid class of drugs. The pharmacological effects of the topical corticosteroids are well known, however, the mechanisms of their dermatologic actions are unclear. Various laboratory methods, including vasoconstrictor assays, are used to compare and predict potencies and/or clinical efficacies of the topical corticosteroids. There is some evidence to suggest that a recognizable correlation exists between vasoconstrictor potency and therapeutic efficacy in man.

**Pharmacokinetics:** The extent of percutaneous absorption of topical corticosteroids is determined by many factors including the vehicle, the integrity of the epidermal barrier and the use of occlusive dressings (see **DOSAGE AND ADMINISTRATION**).

Topical corticosteroids can be absorbed from normal intact skin. Inflammation and/or other disease processes in the skin increase percutaneous absorption. Occlusive dressings substantially increase percutaneous absorption of topical corticosteroids (see **DOSAGE AND ADMINISTRATION**).

Once absorbed through the skin, topical corticosteroids are handled through pharmacokinetic pathways similar to systemically administered corticosteroids. Corticosteroids are bound to plasma proteins in varying degrees. Corticosteroids are metabolized primarily in the liver and then excreted by the kidneys. Some of the topical corticosteroids and their metabolites are also excreted into the bile.

### NYSTATIN and TRIAMCINOLONE ACETONIDE

During clinical studies of mild to severe manifestations of cutaneous candidiasis, patients treated with nystatin and triamcinolone acetonide cream showed a faster and more pronounced clearing of erythema and pruritis than patients treated with nystatin or triamcinolone acetonide alone.

**INDICATIONS AND USAGE**
Nystatin and triamcinolone acetonide cream is indicated for the treatment of cutaneous candidiasis. It has been demonstrated that the nystatin-steroid combination provides greater benefit than the nystatin component alone during the first few days of treatment.

**CONTRAINDICATIONS**
This preparation is contraindicated in those patients with a history of hypersensitivity to any of its components.

**PRECAUTIONS**
**General:** Systemic absorption of topical corticosteroids has produced reversible hypothalamic-pituitary-adrenal (HPA) axis suppression, manifestations of Cushing's syndrome, hyperglycemia, and glucosuria in some patients.
Conditions which augment systemic absorption include the application of more potent steroids, use over large surface areas, prolonged use, and the addition of occlusive dressings (see **DOSAGE AND ADMINISTRATION**).
Therefore, patients receiving a large dose of any potent topical steroid applied to a large surface area should be evaluated periodically for evidence of HPA axis suppression by using the urinary free cortisol and ACTH stimulation tests, and for impairment of thermal homeostasis. If HPA axis suppression or elevation of the body temperature occurs, an attempt should be made to withdraw the drug, to reduce the frequency of application, or to substitute a less potent steroid.
Recovery of HPA axis function and thermal homeostasis are generally prompt and complete upon discontinuation of the drug.
Infrequently, signs and symptoms of steroid withdrawal may occur, requiring supplemental systemic corticosteroids.
Children may absorb proportionally larger amounts of topical corticosteroids and thus be more susceptible to systemic toxicity (see **PRECAUTIONS, Pediatric Use**).
If irritation or hypersensitivity develops with the combination nystatin and triamcinolone acetonide, treatment should be discontinued and appropriate therapy instituted.
**Information for the Patient:** Patients using this medicine should receive the following information and instructions.
1. This medication is to be used as directed by the physician. It is for external use only. Avoid contact with the eyes.

2. Patients should be advised not to use this medication for any disorder other than for which it was prescribed.

3. The treated skin area should not be bandaged or otherwise covered or wrapped as to be occluded (see **DOSAGE AND ADMINISTRATION**).

4. Patients should report any signs of local adverse reactions.

5. When using this medication in the inguinal area, patients should be advised to apply cream sparingly and to wear loose fitting clothing.

6. Parents of pediatric patients should be advised not to use tight-fitting diapers or plastic pants on a child being treated in the diaper area, as these garments may constitute occlusive dressings.

7. Patients should be advised on preventative measures to avoid reinfection.

**Laboratory Tests:** If there is a lack of therapeutic response, appropriate microbiological studies (e.g. KOH smears and/or cultures) should be repeated to confirm the diagnosis and rule out other pathogens, before instituting another course of therapy.
A urinary free cortisol test and ACTH stimulation test may be helpful in evaluating hypothalamic-pituitary-adrenal (HPA) axis suppression due to corticosteroid.
**Carcinogenesis, Mutagenesis, and Impairment of Fertility:** Long term animal studies have not been performed to evaluate the carcinogenic or mutagenic potential or possible impairment of fertility in males or females.
**Pregnancy:**Teratogenic effects —*Pregnancy Category C*: There are no teratogenic studies with combined nystatin and triamcinolone acetonide.
Corticosteroids are generally teratogenic in laboratory animals when administered systemically at relatively low dosage levels. The more potent corticosteroids have been shown to be teratogenic after dermal application in laboratory animals. Therefore, any topical corticosteroid preparation should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
Topical preparations containing corticosteroids should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time.
**Nursing Mothers:** It is not known whether any component of this preparation is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised during use of this preparation by a nursing woman.
**Pediatric Use:** In clinical studies of a limited number of pediatric patients ranging in age from 2 months through twelve years, nystatin and triamcinolone acetonide cream cleared or significantly ameliorated the disease state in most patients.
**Pediatric patients may demonstrate greater susceptibility to topical corticosteroid-induced hypothalamic-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome than mature patients because of a larger skin surface area to body weight ratio.**

HPA axis suppression, Cushing's syndrome, and intracranial hypertension have been reported in children receiving topical corticosteroids. Manifestations of adrenal suppression in children include linear growth retardation, delayed weight gain, low plasma cortisol levels, and absence of response to ACTH stimulation. Manifestations of intracranial hypertension include bulging fontanelles, headaches and bilateral papilledema.
Administration of topical corticosteroids to children should be limited to the least amount compatible with an effective therapeutic regimen. Chronic corticosteroid therapy may interfere with the growth and development of children.

**ADVERSE REACTIONS**
A single case (approximately one percent of patients studied) of acneiform eruption occured with the use of combined nystatin and triamcinolone acetonide in clinical studies.
Nystatin is virtually nontoxic and nonsensitizing and is well tolerated by all age groups, even during prolonged use. Rarely, irritation may occur.
The following local adverse reactions are reported infrequently with topical corticosteroids. These reactions are listed in the approximate decreasing order of occurrence: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin atrophy, striae and miliaria.

**OVERDOSAGE**
Topically applied corticosteroids can be absorbed in sufficient amounts to produce systemic effects (see **PRECAUTIONS, General**). However, acute overdosage and serious adverse effects with dermatologic use are unlikely.

**DOSAGE AND ADMINISTRATION**
Nystatin and triamcinolone acetonide cream is usually applied to the affected areas twice daily in the morning and the evening by gently and thoroughly massaging the preparation into the skin. The cream should be discontinued if symptoms persist after 25 days of therapy (see **PRECAUTIONS, Laboratory Tests**).
Nystatin and triamcinolone acetonide cream should *not* be used with occlusive dressings.

**HOW SUPPLIED**
Nystatin and triamcinolone acetonide cream USP, a yellow to tan cream supplied in:

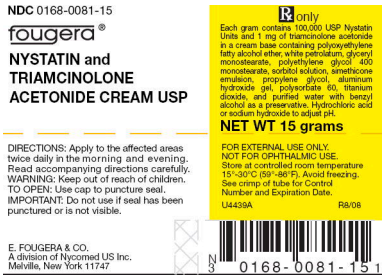
| | |
|---|---|
| 15 gram tube | NDC 0168-0081-15 |
| 30 gram tube | NDC 0168-0081-30 |
| 60 gram tube | NDC 0168-0081-60 |

Store at controlled room temperature 15°-30°C (59°-86°F). Avoid freezing.
**E. FOUGERA & CO.**
A division of Nycomed US Inc.
Melville, New York 11747
I28115G
R3/08
#176

**PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CONTAINER**
NDC 0168-0081-15

Fougera®
**NYSTATIN and**
**TRIAMCINOLONE**
**ACETONIDE CREAM USP**
Rx only
Each gram contains: 100,000 USP Nystatin Units and 1 mg of triamcinolone acetonide in a cream base containing polyoxyethylene fatty alcohol ether, white petrolatum, glyceryl monostearate, polyethylene glycol 400 monostearate, sorbitol solution, simethicone emulsion, propylene glycol, aluminum hydroxide gel, polysorbate 60, titanium dioxide, and purified water with benzyl alcohol as a preservative. Hydrochloric acid or sodium hydroxide to adjust pH.

**NET WT 15 grams**




**PACKAGE LABEL – PRINCIPAL DISPLAY PANEL – 15 G CARTON**

NDC 0168-0081-15

Fougera® Rx only

**NYSTATIN and TRIAMCINOLONE ACETONIDE CREAM USP**

**WARNING: Keep out of reach of children.**

FOR EXTERNAL USE ONLY.

NOT FOR OPHTHALMIC USE.

**NET WT 15 grams**